

Remarks

Claims 1-3, 7, 8 and 12-15 are pending in the application. No claims have been allowed.

Claims 9-10 have been cancelled by this amendment.

Claims 1 and 12 have been amended. More specifically, the term “wherein the formulation is spot-on or pour-on” has been incorporated in Claims 1 and 12. The amendments to Claims 1 and 12 are at least supported by cancelled Claims 9 and 10 as well as page 8, lines 25-33 and page 9, lines 1-13 of the specification.

Claim 15 has been amended to incorporate the limitation “by a spot-on or pour-on protocol.” The amendment to Claim 15 is at least supported by Claims 9 and 10 as well as page 8, lines 25-33 and page 9, lines 1-13 of the specification.

Applicants respectively contend the amendments are fully supported by the specification in the present application and do not add new matter. Applicants request entry of these amendments as they place the claims in position for allowance or in better form for appeal.

All pending claims stand rejected under 35 U.S.C. 103(a) over Watson et. al. (U.S. 6,235,754 B1) in view of Bosserelle (U.S. 4,740,432) and JP 03251520.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to the skilled artisan to modify or to combine the reference teachings to achieve the claimed invention with a reasonable expectation of success, and the combined references must teach or suggest all the limitations of the claimed invention. Applicants respectfully contend the combination of references referring to the term shampoo as applied by the Examiner does not provide one skilled in the art a teaching or suggestion that supports the judicious selection and use of specific elements from the prior art with an expectation of success to achieve the presently claimed combination. The individual prior art references generally contain a broad range of variables within their definitions and nothing to suggest a selection and use of a single element from each of those references in combination. Applicants further contend that one skilled in the art would not be motivated to combine the references referring to the term shampoo to solve the problem that the instant invention addresses. It is Applicants’ position a *prima facie* case of obviousness has not been established against the presently claimed invention.

Watson et. al. generally discloses methods and compositions for treating animals and humans for controlling infestation by arthropods and helminths by administering a 1,4-diaryl-

2-fluoro-2-butene or 1,4-diaryl-2,3-difluoro-2-butene compound having the structural formula and definitions recited in the reference. As provided in this reference, there is a significant list of optionally defined substituents at each of the variable positions on the compound having structural formula I.

At column 4, lines 54-67 and column 5, lines 1-37 there is a disclosure of a host of various parasites against which the compositions and methods are said to be useful as well as a listing of animals and humans on which the methods and compositions are said to be useful.

At column 5, line 49, spinosads are mentioned along with numerous other parasiticides including anthelmintics, endectocides, ectoparasiticides, insect growth regulators and chitin synthesis inhibitors. The spinosads are mentioned within the group referred to as gamma-butyric acid inhibitors.

It should be recognized that no special significance or preference is expressed in Watson for the inclusion of a second active agent, much less particularizing a class or a named second active agent to be combined with the 1,4-diaryl-2-butene or 1,4-diaryl-2,3-difluoro-2-butene compound that are the mandatory active agents for inclusion in the composition and the methods of Watson et. al.

In a similar manner, shampoo is listed at column 5, line 64 along with numerous other forms of compositions that are said to be suitable for topical administration to animals and humans. At column 6, lines 3-11, oral, intragastric, intraruminal and parenteral routes of administration are also mentioned. Once again, no preference, shampoo or otherwise, is mentioned in Watson et. al. for a particular route of administration or a compositional form for a particular route of administration.

Applicants respectfully contend the Watson et. al. reference contains no teaching or suggestion that supports the selection and use of a particular formulation type for administration by particular route of administration as a preference over any other formulation type or route of administration. Further, there is nothing in Watson et. al. to suggest the particular active agents, formula I, could or should be omitted in favor of an alternative active agent. Rather, the disclosure in Watson et. al. clearly suggests the inclusion of a second active agent drawn from a vast number of parasiticides is merely an option. No particular significance or preference is expressed for the inclusion of a second active agent or which of the vast classes or specific active agents might be preferred.

Bosserelle generally discloses cosmetic compositions, one of which is a shampoo, that contain "triglycerides of fatty acids." The problem that Bosserelle is addressing is a substitute for animal origin fatty substance compositions such as mink oil, marmot oil and green turtle oil for cosmetic composition uses. Bosserelle's disclosed solution to this problem is to utilize, or substitute, vegetable origin fatty substance compositions. The composition that Bosserelle discloses as useful in cosmetics as a substitute for the animal origin fatty substance is a vegetable origin fatty substance composition containing: 1) fatty

acid triglycerides; 2) fatty acid ester containing 40 carbon atoms; 3) vitamins; 4) and an antioxidant if required. The whole of the vegetable origin fatty substance composition is referred to as "chelonine." In addition to further describing and defining the fatty acid esters containing 40 carbon atoms, the vitamins and the antioxidant, Bosserelle also further defines the fatty acid triglycerides. The triglycerides are, of course, esters of a fatty acid(s) and glycerol where all three hydroxyl groups of glycerol are esterified with a fatty acid of varying carbon chain length. In Bosserelle, the fatty acid composition of the glycerol esters are described as comprising varying percentages of myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, and oleic acid. Each of these acids, by definition, is esterified with glycerol to afford the fatty acid triglyceride portion of the vegetable origin fatty substance composition.

Applicants respectfully contend there is no teaching or suggestion that supports the selection of oleic acid in the absence of being esterified with glycerol along with other fatty acids, removing it from the shampoo composition, and using it in the compositions of the present invention, or in the 1,4-diaryl-2(or 2,3)-fluoro or difluoro-2-butene compound containing compositions of Watson et. al. as a single element.

Reference JP 03251520 generally discloses a composition for shampoo containing at least four components; (1) one or more ampholyte surfactants; (2) one or more nonionic surfactants; (3) one or more of silicon derivatives of dimethyl polysiloxane, methylphenyl polysiloxane, fatty acid-modified polysiloxane, aliphatic alcohol-modified polysiloxane, polyoxy alkylene-modified polysiloxane, amino-modified polysiloxane and cation-modified polysiloxane; and (4) an oil-component of hydrocarbons. More particularly, component (1) is betaine-type (carboxy betaine or sulpho betaine), or amide betaine surfactant; (2) is polyoxy ethylene alkyl ether, alkyl allyl, polyoxy ethylene ether, or polyoxy ethylene alkyl amine; (3) is polyoxy alkylene-modified polysiloxane having an average molecular weight of 3000 or more; and (4) is an animal or vegetable oil (such as corn oil, olive oil, or mink oil, ester oil such as isopropyl myristate or isopropyl palmitate, or hydrocarbons such as fluid paraffin or squalene). Even more particularly, in an example, imidazolinium betaine (10 weight percent), polyoxy ethylene (10 mol) nonyl phenyl ether, fluid paraffin, dimethyl polysiloxane, and water are formed into a shampoo. Clearly, the component (4) used in the example was drawn from hydrocarbons oil component group rather than animal oil, vegetable oil, or ester oil.

Applicants contend that the skilled artisan would recognize that reference JP 03251520 is an English language abstract derived from the original Japanese patent application of the same number. Applicants further content that the skilled artisan would

recognize that as a derived abstract, the JP 03251520 reference is limited in its representation of the full disclosure and as such would seek the application for the complete teaching. Applicants respectfully submit a machine based translation of JP 2837489B2 in the English language. Reference JP 2837489B2 is a patent within the family of application JP 03251520 and as such represents the intended teaching of the abstract derived from JP 03251520 as viewed by the skilled artisan.

Reference JP 2837489B2 like reference JP 03251520 generally discloses a composition for shampoo containing at least four components; (1) one or more ampholyte surfactants; (2) one or more nonionic surfactants; (3) one or more of silicon derivatives of dimethyl polysiloxane, methlyphenyl polysiloxane, fatty acid-modified polysiloxane, aliphatic alcohol-modified polysiloxane, polyoxy alkylene-modified polysiloxane, amino-modified polysiloxane and cation-modified polysiloxane; and (4) one or more selected from one or more kinds of a oil-component of hydrocarbons. See patent, page 3, Claim 1. More particularly, over 150 examples of (4) oil components are presented from the groups: an animal or vegetable oil, a higher alcohol, a higher aliphatic acid and a synthetic ester. See patent, page 6, third paragraph through page 7, second paragraph. Included in the description of synthetic esters is isopropyl myristate, the first entry of 50 examples given. With no preference indicated for synthetic esters, the skilled artisan would deduce that isopropyl myristate was selected for the abstract simply on the basis that it occurred first in the list of 50 examples.

Applicants respectfully contend there is no teaching or suggestion that supports the selection and use of isopropyl myristate from the four-component composition of JP 2837489B2 from among the over 150 examples of oil components for agents generally described as useful in the shampoo compositions and combine it with further elements to arrive at the presently claimed invention with a reasonable expectation of success.

Applicants respectfully contend the Examiner has chose to combine the references based on the common occurrence of the term shampoo and as such has misconstrued the Applicants' invention to be a shampoo. As stated above, shampoo compositions are topical treatments that distinguish themselves from the Applicants' invention by the elements making up the composition. In addition, shampoo compositions are distinguished by their required actions of application. Applicants respectively direct the Examiner to attachment A, Principles of Topical Therapy, The Merck Veterinary Manual, pages 600 through 601 ("Merck"). "Merck" represents reasonably contemporaneous knowledge in the art at the time of filing in that it predates the present application's filing date by one year.

“There are three broad classes of shampoos: cleansing, antiparasitic, and medicated. Cleansing shampoos remove dirt and excess oils from the coat. These products include over-the-counter dog grooming shampoos, flea shampoos, and many mild products for people. These products lather well and must be rinsed from the coat. Antiparasitic shampoos are “flea shampoos.” In most cases, the amount of insecticide in these products is not adequate to kill all of the fleas in a severe infestation. However, these products are excellent routine cleansing products.” See attachment A.

Applicants contend that the skilled artisan would recognize that shampoo compositions are formulated primarily for cleansing which includes the necessary step of rinsing and as such would not be motivated to look to the shampoo art for the spot-on or pour-on ectoparasiticide formulation of the instant invention.

Applicants further contend that the skilled artisan would recognize antiparasitic shampoos compositions are not believed adequate against flea infestation and as such would not be motivated to combine the references to solve the problem that the instant invention addresses. Applicants remind the Examiner that the instant invention provides the advantage of an effective treatment of ectoparasite infestation by migration or spreading over the entire surface of the animal from the application of a composition of Claim 1 on a narrow strip of the animal's dorsal midline and as such is distinct from shampoo and its required actions of application.

Applicants respectfully contend the prior art references as applied by the Examiner require a selective combination from among isolated disclosures in the prior art with no teaching or suggestion of preferences for any of those elements in order to approach arriving at Applicants' claimed invention.

Applicants respectfully contend the Examiner has picked and chosen non-preferred elements from prior art compositions to arrive at an obviousness rejection in the present case. None of the references contain a teaching or suggestion that supports the selection and use of the individual elements with an expectation of success to achieve the presently claimed combination.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to the skilled artisan to modify or to combine the reference teachings to achieve the claimed invention with a reasonable expectation of success, and the combined references must teach or suggest all the limitations of the claimed invention. Applicants respectfully contend the combination of references referring to the term shampoo as applied by the Examiner does not provide one skilled in the art a teaching or suggestion that supports the judicious selection and use of specific elements from the prior art with an expectation of success to achieve the presently claimed combination. The individual prior art references generally contain a broad range of variables within their definitions and nothing to suggest a

selection and use of a single element from each of those references in combination. Applicants further contend that one skilled in the art would not be motivated to combine the references referring to the term shampoo to solve the problem that the instant invention addresses. It is Applicants' position a *prima facie* case of obviousness has not been established against the presently claimed invention

In view of the previous amendments to the claims and the remarks made herein, Applicants respectfully favorable reconsideration of this application.

Respectfully submitted,



John C. Demeter
Attorney for Applicants
Registration No. 30,167
Phone: 317-276-3785

Eli Lilly and Company
Patent Division/JCD
P.O. Box 6288
Indianapolis, Indiana 46206-6288

July 29, 2004